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Insulin Treatment after 3 Years in Patients with Type 2 Diabetes Following Participation in a Study of Combination Regimes of Insulin, Repaglinide and Metformin

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Many short-term studies of insulin initiation in Type 2 Diabetes have been undertaken, but there is little long-term data regarding the durability of the initiating insulin regime. We report the three-year follow-up of 82 patients randomised to a study comparing Human Mixtard and metformin (n=27), bedtime Human Insulatard and metformin (n=26), and bedtime Human Insulatard with metformin and repaglinide (n=25). At 36 months, 78%, 15% and 20% respectively remained on the initiating insulin regime. The most common regimes after 3 years were twice-daily insulin mixtures (n=38) and basal bolus therapy (n=18). The mean HbA1c were 8.2% and 8.8% respectively, while 47.1% and 16.7% were achieving a mean HbA1c <7.5%. The mean HbA1c was 7.5% for patients initiated on twice-daily Human Mixtard and 8.8% for patients transferred to twice-daily insulin mixtures (60.0% and 28.6% achieved HbA1c <7.5% respectively). The mean HbA1c fall in patients transferring to insulin mixtures was 1.5% (10.3% vs 8.8%), and 1.1% in patients transferring to basal bolus therapy (9.9% vs 8.8%). These results suggest that twice-daily Human Mixtard and metformin provides sustained glycaemic control as the initiating insulin, but tight glycaemic control is more difficult to achieve if glycaemic control deteriorates on the initiating insulin regime.

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Dicarbonyl Derived AGEs Are Decreased by Reducing Post Prandial Glucose Levels

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The relative importance of fasting and postprandial hyperglycemia (PPH) to vascular dysfunction in diabetes remains controversial. Proteins modified by glycation and oxidative stress undergo proteolysis with release of corresponding free adducts, particularly hydroimidazolones (F-HI), which are increased 10-15-fold in urine and plasma in diabetes. Since decreasing PPH with insulin Lispro (LP) decreases PP glucose, methylglyoxal (MG), and 3-deoxyglucosome (3DG) relative to regular insulin (RI) we have studied MG and 3DG derived F-HI (MG-HI and 3DG-H) and free carboxymethyllysine (F-CML) and carboxyethyllysine (F-CEL) during LP and RI treatment.

Free MG-HI, 3DG-H, CEL and CML, measured by LC-MS/MS, and HbA1c, were determined in urine and plasma at 2 mos. intervals in a randomized 4 mos. LP/RI crossover study of 21 subjects with type 1 diabetes.

Plasma F-3DG-H was significantly reversed (23%) by LP therapy, while plasma F-MG-H1 was decreased by 24%, although these changes were just non-significant (NS). F-CML was also significantly reversed (19%) by LP therapy, while F-CEL was reversed 11% by LP therapy (NS).

Urinary levels of F-MG-HI and 3DG-H were significantly reversed (13% and 19%) by LP as was F-CML (19%). F-CEL was also reversed by LP, although this change was just NS. HbA1C levels were not affected by LP treatment.

We conclude that the profound increases in selected MG-, 3DG- and glyoxal-derived advanced glycation endproducts seen in diabetes are responsive to decreasing postprandial hyperglycemia proportionate to fractional total glucose and alpha-dicarbonyl exposure.

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Three Year Prospective Parallel Trial in 2 Groups of Patients with Type 2 Diabetes and Cardiovascular Disease and the Utilization of Rosiglitazone; One Year Interim Analysis

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Coronary artery disease (CAD) represents a major cause of morbidity and mortality in patients with type 2 diabetes. The insulin sensitizer and peroxisome proliferator-activated receptor-γ (PPAR-γ) ligand rosiglitazone (RSG) has been shown to improve endothelial function in human studies.

One year interim analysis was performed on this three year non-randomized open label, parallel trial. The primary endpoints of this trial are all cause mortality and composite CAD events. Patients with CAD or CAD equivalent(s) were given the choice of participating in an outpatient diabetes program which aggressively utilized RSG in all medical candidates (intensive group, n= 38) or receive usual care with their primary care physicians (usual care group n=52).

Both the intensive and control groups had similar baseline characteristics: BMI , age, duration of diabetes and metabolic syndrome. (p = NS) Baseline cholesterol, HbA1c and blood pressure were similar. (p = NS) The intensive group, however utilized significantly more RSG (intensive 50% versus control 19%, p<.003). Metformin, sulfonylurea and insulin usage was similar. At one year, no differences were seen in either groups with cholesterol levels. Blood pressure was lower in the intensive group (p=.006) and glucose control was lower but not significantly (HbA1c intensive 7.1 versus control 7.9, p = .28). All cause mortality was significantly lower in the intensive group (Intensive = 0 deaths, control = 9 deaths, p = .001) No differences in composite cardiovascular outcomes seen yet (intensive = 5 events, control = 4 events, p = NS). Significant improvements in all cause mortality at one year were observed in intensive group which utilized significantly more RSG and experienced lower blood pressure at one year. Further prospective follow-up is warranted.

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Antioxidant Effects of Carvedilol and Alluporinol in Patients with Diabetes Type II; A Randomized, Double-Blind Placebo-Controlled Clinical Trial

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Background: Diabetes type II is associated with oxidative stress while Carvedilol and Allopurinol has been shown to have antioxidant properties, which are thought to account for the protective effects. Objective of this study was to compare the short-term effects of Carvedilol, Allopurinol and placebo on oxidative stress status in patients with diabetes type II.

Material and methods: Eighty one patients were randomly assigned to four different groups: Carvedilol (6.25 mg TDS, n=20), placebo (n=20) and Allopurinol (100 mg TDS, n=20), placebo (n=21). The patients were received their treatment for two weeks. Fasting blood sugar (FBS), HbA_1c, total antioxidant capacity (FRAP test) and lipid peroxidation (TBARS assay) in plasma and saliva were measured before and after treatment.

Results: No significant differences in oxidative stress status, FBS and HbA_{1C} were seen among placebo and Carvedilol groups, and also in HbA_{1C} and FBS levels between Allopurinol and placebo group.

Conclusion: It is concluded that Allopurinol and Carvedilol are not more effective than placebo in reduction of oxidative stress in diabetic patients. However, to elaborate the exact role of Allopurinol and Carvedilol in diabetes, further large randomized clinical trials with longer time are needed. The same trend of changes in blood and saliva shown for oxidative stress indices was interesting and suggests a chance for saliva to be valuable in diagnosis of oxidative stress.

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Design of an Outpatient Hyperglycemia Protocol for Use in a Primary Care Setting

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The Family Medicine Center (FMC) is a free standing outpatient clinic on the University of Oklahoma Health Sciences Center campus. It houses a family medicine residency training program and it serves a patient population that is approximately 50% Medicaid. The FMC has a diabetes co-management service that is recognized by the American Diabetes Association as an education program. The FMC's diabetes advisory board identified the need for a standardized way to address acute hyperglycemia. The advisory group recommended forming a separate subcommittee to address this issue. The charge of the subcommittee was to develop an outpatient hyperglycemia protocol for facility wide use. The subcommittee met on three occasions. The subcommittee was composed of three family medicine attending physicians, a clinical pharmacist, lab technician, nurse, and a physician assistant. A literature search was performed to determine if a similar protocol already existed. Numerous emergency room based treatment protocols and algorithms were found that addressed the appropriate work-up and treatment of diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) but no specific outpatient protocol could be found. An outpatient hyperglycemia protocol was created in two parts. The first is a two page reference tool to guide clinicians in medical decision making. It includes

For author duality of interest information, see page A787.